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August 2, 2002

CERTIFICATE OF MAILING
37 C.F.R. § 1.8

I hereby certify that this correspondence is being deposited with the U.S. Postal Service as First Class Mail in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231, on the date below:

August 2, 2002
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Mark B. Wilson

BOX AF
Commissioner of Patents
Washington DC 20231

Re: SN 09/339,352 "ABSORPTIVE HYPERCALCIURIA LOCUS ON CHROMOSOME 1" - Reed-Gitomer et al. (Client Ref. UTSMC:DAL0553)
Matter No. 10017634/UTSD:553

Commissioner:

Transmitted herewith for filing are:

1. Reply Brief with Appendix A(original and 2 copies);

2. Request for Oral Argument (original and 2 copies);

3. Check in the amount of $140.00 in payment of the required fee for the Request for Oral Argument for a small entity;

4. A return postcard to acknowledge receipt of these materials. Please date stamp and mail this postcard.

If the check is inadvertently omitted, or should any additional fees be required under 37 C.F.R. §§ 1.16 to 1.21 for any reason relating to the enclosed materials, the Commissioner is

authorized to deduct said fees from Fulbright & Jaworski Deposit Account No. 50-1212/UTSD:553.

Very truly yours,

Mark B. Wilson

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Enclosures

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Berenice Y. Reed-Gitomer
Charles Y.C. Pak

Serial No.: 09/339,352

Filed: June 23, 1999

For: ABSORPTIVE HYPERCALCIURIA LOCUS ON CHROMOSOME 1

Group Art Unit: 1663

Examiner: H. Robinson

Atty. Dkt. No.: UTSD:553/MBW

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REPLY BRIEF

Reed/Gitomer/Robinson

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Berenice Y. Reed-Gitomer
Charles Y.C. Pak

Serial No.: 09/339,352

Filed: June 23, 1999

For: ABSORPTIVE HYPERCALCIURIA LOCUS ON CHROMOSOME 1

Group Art Unit: 1653

Examiner: H. Robinson

Atty. Dkt. No.: UTSD:553/MBW

REPLY BRIEF

BOX AF
Commissioner of Patents
Washington, D.C. 20231

Sir:

Appellants hereby submit an original and two copies of this Reply Brief to the Board of Patent Appeals and Interferences in response to the Examiner's Answer ("the Answer") mailed June 3, 2002.

It is believed that no fees under 37 C.F.R. §§ 1.16 to 1.21 are occasioned by the filing of this paper; however, should the Commissioner determine otherwise, the Commissioner is hereby authorized to deduct said fees from Fulbright & Jaworski Deposit Account No. 50-1212/UTSD:553.

I. REAL PARTY IN INTEREST

The real party in interest is the assignee, Board of Regents, The University of Texas System, Austin, Texas.

II. RELATED APPEALS AND INTERFERENCES

There are no interferences or appeals for related cases.

III. STATUS OF THE CLAIMS

Claims 1-26 were originally filed in the present application. During prosecution, claims 8-9, 16 and 18-26 were cancelled and claims 1, 10, 11 and 12 were amended. Accordingly, claims 1-7, 10-15 and 17 are pending. Of these, claims 1-7, 10-15 and 17 are the subject of the present appeal and stand appealed. A copy of the appealed claims is attached as Appendix A to this Brief.

The Answer alleges that claim 12 has been improperly presented for appeal. The Answer suggests in an Appendix to the Answer a version of claim 12 allegedly in proper form. However, Appellants note that the Answer's version of claim 12 is in error. The suggested version of claim 12 recites "SEQ ID NO: &" rather than properly reciting "SEQ ID NO: 7." Appellants respectfully point out that as claim 12 exists in the record it has never contained such an error until now. Appellants therefore respectfully submit that the properly presented claim 12 recites SEQ ID NO: 7, as provided in the Appeal Brief and in Appendix A to this Reply Brief.

Additionally, the version suggested in the Answer omits a comma after the phrase "GenBank Accession #Z97876." Although the Answer does not specify that this comma is the

substance of the improper presentation of claim 12, Appellants can find no other errors. The proper claim 12 is included in the copy of the appealed claims in the present Appendix A.

IV. STATUS OF AMENDMENTS

Appellants have made no amendments subsequent to the final rejection.

V. SUMMARY OF THE INVENTION

Appellants agree that the summary of the invention as contained in the Brief is correct.

This invention involves Appellants' discovery of an area on human chromosome 1 that is genetically linked to hypercalciuria in general and absorptive hypercalciuria in specific. *See* Specification, p. 5, lns. 27-30, p. 6, lns. 1-15. The specific area of chromosome 1 involved in the invention is that region containing 1q23 and 1q24. *See* Specification, p. 6, lns. 12-30. This discovery allows one to screen subjects and determine if the subject has an increased risk of absorptive hypercalciuria. The screening methods generally comprise obtaining a sample of nucleic acid from a subject and analyzing the sample of nucleic acid to detect the presence or absence of a genetic mutation in the genomic region of chromosome 1. The presence of such a mutation indicated in increased risk of hypercalciuria; the absence of such a mutation does not indicate an increased risk. *See* Specification, p. 6, lns. 11-19. The nucleic acid can be analyzed using standard techniques well known and used by those of ordinary skill in the art, for example, PCR, diagnostic RFLP analysis, RNase protection assay or RNase mismatch cleavage.

VI. ISSUES ON APPEAL

The issues for the Board's consideration are:

(1) Whether claims 1-7, 10-15 and 17 are properly rejected under 35 U.S.C. § 101 as lacking a specific and substantial asserted utility or a well established utility.

(2) Whether claims 1-7, 10-15 and 17 are properly rejected under 35 U.S.C. § 112, first paragraph, as lacking a specific utility to enable one skilled in the art to use the claimed invention without undue experimentation.

Appellants note the withdrawal of the rejection of claims 1-7, 10-15 and 17 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Appellant regards as the invention.

VII. GROUPING OF THE CLAIMS

For purposes of this Appeal, the claims should stand or fall separately. The Answer agrees that reasons for separate patentability have been provided under 37 C.F.R. §1.192(c)(7) and (c)(8). For convenience, Appellants reiterate those reasons here.

For the purpose of the rejection under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph, claim 2 should stand or fall separately from the remainder of the claims. Claim 2 is directed specifically to the determination of whether or not an individual has an increased risk of developing absorptive hypercalciuria, instead of hypercalciuria of any form. The majority of the data in the specification and the Declaration of Charles Y.C. Pak and Berenice Y. Reed-Gitomer, submitted as Appendix B in the Appeal Brief, relates specifically to an increased risk of absorptive hypercalciuria. These data are discussed in the Appeal Brief and below. Therefore, although Applicants submit that such a determination would not be supported by the facts of this

case, the Board could determine that a claim of the scope of present claim 1 is properly rejected under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph, while a claim limited in scope to absorptive hypercalciuria is not properly rejected under these grounds.

VIII. ARGUMENT

A. Claims 1-7, 10-15 and 17 Have an Asserted Utility

As discussed in detail below, the claimed invention has an asserted utility for the following reasons:

- **An Applicant's assertion of utility is presumed true and sufficient to satisfy the utility requirement of 35 U.S.C. §101.**
- **Applicants have asserted that the specific utility is the use of the 1q23.3-1q24 locus in screening for an increased risk of developing hypercalciuria.**
- **The Examiner's contention that there is no substantial utility is mere speculation.**

The Action rejects claim 1 under 35 U.S.C. §101 asserting that "the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility based on screening for increased risk of developing hypercalciuria." The Examiner contends that the specification does not clearly set forth how a standardized screening method would be developed to screen for increased risk of absorptive hypercalciuria (AH). The Examiner also contends that the uncertainty of the gene region and variability of the mutation, may be indicia of a "real world" use, but in view of the absence in the application of working examples and

complete details for carrying out the processes indicated in the claims, the utility indicated would require further experimentation. Appellants traverse this rejection.

Both the Federal Circuit Court and the Court of Customs and Patent Appeals have directed the Patent Office to presume that an Applicant's assertion of utility is true and is sufficient to satisfy the utility requirement of 35 U.S.C. §101. *See* e.g., *In re Jolles*, 628 F.2d 1322, 206 USPQ (CCPA 1980); *In re Irons*, 340 F.2d 974, 144 USPQ 351 (CCPA 1965); *In re Langer*, 503 F.2d 1380, 183 USPQ 288 (CCPA); *In re Sichert*, 556 F.2d 1154, 1159, 196 USPQ 209-212-13 (CCPA 1977).

Appellants have clearly asserted the utility of the claimed invention. The specification at page 6, lines 11-15, states that: "[d]escribed in this invention is a method for screening for an increased risk of hypercalciuria by obtaining a sample nucleic acid from a subject; and analyzing the sample nucleic acid to detect the presence or absence of a genetic mutation in genomic region associated with an increased risk of developing hypercalciuria." The specific utility asserted by the application is thus the use of the claimed locus in screening for an increased risk of developing hypercalciuria. A person of ordinary skill would find this a credible assertion. The instant invention sets forth a genetic locus that is statistically related to an absorptive hypercalciuria (AH) phenotype in the screened kindred groups. The detection of the altered loci would determine an individual at risk and would facilitate early detection of disease onset and potential intervention to allow for modifications in lifestyle or diet that could prevent or delay onset of the disease.

Any contention of a "*lack of asserted utility*" simply does not withstand an examination of the facts. The specification clearly discloses a specific genomic region of chromosome 1, 1q23.3-1q24, that is reasonably correlated to a specific disease condition, hypercalciuria, in

particular absorptive hypercalciuria (AH). The inventors established a statistically significant linkage between an alteration in this loci and the AH phenotype. The Answer has not provided any additional reason to doubt the asserted utility.

The Examiner's mere contention that it would be undue experimentation due to the absence of data is merely speculation by the Examiner. The Examiner appears to assert more knowledge than the skilled artisans and thus, is substituting her judgment for that of an established expert in the art. This is improper. *In re Zeidler*, 682 F.2d.961, 966-967 (Fed. Cir. 1982). Appellants assert that the Office must provide specific, evidentiary scientific basis (e.g., scientific journal articles, or excepts form patents or scientific treatises) for its factual conclusions that the present invention "lacks an asserted utility."

Therefore, in view of the arguments that one of skill in the art would reasonably recognize a correlation between the asserted utility and the ability to screen for AH as the instant specification sets forth, Appellants respectfully request that the Board overturn the rejection of the claims for "lack of utility."

B. Claims 1-7, 10-15 and 17 Are Enabled

As discussed in detail below, claims 1-7, 10-15 and 17 are enabled for the following reasons:

- **The rejection is without support and is founded in the rejection for lack of utility.**
- **The burden of proof has been erroneously placed upon the Appellants without offering any evidence or reasoning based on the record as a whole why the disclosure is not enabling for the pending claims.**

- **Linkage analysis was performed in order to establish the correlation between hypercalciuria and the disclosed locus.**

- **A person of ordinary skill may readily develop methods of screening for defects within the disclosed locus based upon this linkage analysis.**

The Action rejects claims 1-7, 10-15 and 17 under 35 U.S.C. 112, first paragraph, asserting that "the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility" and thus a person of ordinary skill would not know how to use the invention without undue experimentation. In the Action, the Examiner also reinstated her contentions that the specification is not enabled for one skilled in the art to make and use the claimed invention. The Action contends that the claimed invention is enabled for the nucleic acid sequence of SEQ ID NO: 1 that encodes a protein contained in SEQ ID NO:2, however, does not provide enablement for any hypercalciuria gene nor a screening method for "increased risk" of AH. Appellants respectfully traverse this rejection.

The burden of proof has been erroneously placed upon the Appellants without offering any evidence or reasoning based on the record as a whole why the disclosure is not enabling for the pending claims. The single "grounds" of rejection is without support and is couched in terms that a person of ordinary skill would not be enabled to carry out the invention because one of ordinary skill would have no way of recognizing a utility for the invention. This is wrong.

The instant specification sets forth a means for screening for hypercalciuria. Linkage analysis was performed in order to establish the correlation between the AH phenotype and the disclosed loci. A person of ordinary skill would understand that similar means to those taught by the specification could be employed to screen for the altered loci in other individuals deemed to

be at risk for the development of the disease, *i.e.*, based on family history, as the specification teaches a successful means of screening (*see* examples 1 and 2).

No undue experimentation is needed to practice the invention, because Appellants' disclosure clearly enables a screening method for determining an individual with an "increased risk" of the AH phenotype. A person of ordinary skill could readily develop methods of screening for defects within the disclosed region.

The Answer has not provided any additional support in rejection such as published references or Examiner's Affidavit. Furthermore, even though an application need not include working examples in order to be enabled, *In re Borkowski*, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA), the Application does provide a working example that correlates specific mutations located in the chromosome 1q24 locus to the AH phenotype. Although not required, the existence of such a working example should not be dismissed for being inadequate. Additionally, as discussed in Appellants' Brief, the inventors have submitted, in the form of a declaration, new data that even further establish the utility and enablement of the invention.

In view of the above and the facts and arguments of record, Appellants request that the Board overturn the enablement rejection.

C. Claim 2 is Separately Patentable over all Rejections

As discussed in detail below, the claim 2 is separately patentable for the following reasons:

- **Claim 2 has a more specific utility – to screen for increased risk of *absorptive* hypercalciuria.**

- **The utility of the invention of claim 2 is firmly supported by specific data correlating mutations in the locus to absorptive hypercalciuria.**

In addition to the above arguments, which apply to all of the claims, Applicants have further argued that the subject matter of current claim 2 has utility for even additional reasons. The Answer fails to specifically address these arguments, although the Answer agrees that reasons for the separate patentability of claim 2 have been provided.

Claim 2 is directed specifically to determining whether or not one has an increased risk of absorptive hypercalciuria, the specific form of hypercalciuria about which the inventors have gathered the most information. Although Appellants submit that they have shown that the invention has utility in regard to determining whether or not one has an increased risk of hypercalciuria in general, it is possible that the Board could disagree with this broad of a utility. Appellants have argued that there are additional and compelling arguments for the utility of the subject matter of claim 2, since all of the mutations which have been found to result in hypercalciuria have also been specifically linked to absorptive hypercalciuria. Therefore, even if the Board does not find the subject matter of claim 1 to have utility, the subject matter of claim 2 should be found to have utility.

Appellants' arguments have not been countered or addressed in the Answer. In view of the above and the facts and arguments of record, Appellants request that the Board overturn the utility rejection for claim 2.

D. Priority to the Provisional Filing Date

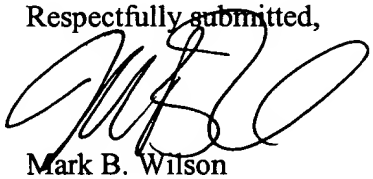
Appellants agree with the Answer that the issue of claim of priority is not appealed. Indeed, Appellants have argued that the issue has always been irrelevant to the rejections of

record and have queried why the issue was raised in the first instance since no art is cited in rejection. Appellants respectfully submit that the allegation as first raised, and now dropped upon appeal, is improper in any event.

IX. CONCLUSION

Appellants have provided arguments in the Appeal Brief and in this Reply Brief that overcome the pending rejections. Appellant respectfully submits that the conclusions that the claims should be rejected are unwarranted. It is therefore requested that the Board overturn the rejections.

Respectfully submitted,



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A

APPENDIX A: Claims on Appeal

1. A method for screening for an increased risk of hypercalciuria comprising:
   (a) obtaining a sample nucleic acid from a subject; and
   (b) analyzing the sample nucleic acid to detect the presence or absence of a genetic mutation in a genomic region associated with an increased risk of developing hypercalciuria, wherein said genomic region is comprised in chromosome 1q23.3-1q24.

2. The method of claim 1, wherein the hypercalciuria is further defined as absorptive hypercalciuria.

3. The method of claim 1, wherein the hypercalciuria is further defined as osteoporosis with hypercalciuria.

4. The method of claim 3, wherein the osteoporosis with hypercalciuria is further defined as idiopathic osteoporosis with hypercalciuria.

5. The method of claim 3, wherein the osteoporosis with hypercalciuria is further defined as postmenopausal osteoporosis with hypercalciuria.

6. The method of claim 1, wherein the nucleic acid is DNA.

7. The method of claim 1, wherein the subject is a human.

10. The method of claim 1, wherein the genomic region is located between markers D1S2681 and D1S2815.

11. The method of claim 1, wherein the genomic region has a sequence contained in SEQ ID NO:1.

12. The method of claim 1, wherein the genomic region has a sequence contained in at least one genetic sequence selected from the group consisting of the genetic sequences set forth in GenBank Accession # Z97876 (SEQ ID NO: 7, SEQ ID NO: 8 and SEQ ID NO: 9), GenBank Accession # Z99943 (SEQ ID NO: 10), and GenBank Accession # AL031733 (SEQ ID NO: 7).

13. The method of claim 1, wherein the genomic region has a lod score of greater than 3.0 but less than 30.0.

14. The method of claim 1, wherein analyzing the sample nucleic acid is done with a PCR procedure, diagnostic RFLP analysis, RNase protection assay, or RNase mismatch cleavage assay.

15. The method of claim 14, wherein analyzing the sample nucleic acid is done with a PCR procedure.

17. The method of claim 15, wherein the screening for an increased risk of hypercalciuria comprises:

(a) obtaining a sample nucleic acid from a subject; and

(b) analyzing the sample nucleic acid to detect the presence or absence of a genetic mutation in genomic region associated with an increased risk of developing hypercalciuria.